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"Express Mail" Label No.: EV053177132US
Date of Deposit: 12/04/2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Alexander H. Borchers and Kenneth W. Dobie

For: Antisense Modulation of Hematopoietic cell protein tyrosine kinase
Expression

BOX SEQUENCE

Assistant Commissioner for Patents
Washington DC 20231

PATENT APPLICATION TRANSMITTAL LETTER

Transmitted herewith for filing, please find the following:

- The specification of the above-referenced patent application;
- An **executed** Declaration or Oath and Power of Attorney;
- An Assignment of the invention to **Isis Pharmaceuticals Inc.** with recordation cover sheet (PTO Form PTO-1595) and \$40.00 cover fee;
- Statement to Support Filing and Submission of DNA/Amino Acid Sequences in Accordance with 37 CFR § § 1.821 through 1.825;
- Sequence listing in computer readable form in accordance with 37 C.F.R. § 1.821(e);
- An Information Disclosure Statement with references; and
- Applicant claims small entity status pursuant to 37 CFR § 1.27.

The filing fee has been calculated as shown below:

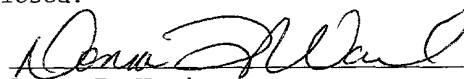
For:	No. Filed	No. Extra	Rate	Fee
BASE FEE				\$370.00
Total Claims	20 - 20 =	0	X \$9=	\$0
Indep. Claims	2 - 3 =	0	x\$40=	\$0
			TOTAL	\$ 370.00

The Commissioner is hereby authorized to charge the following fees to Deposit Account No. 500252:

- the amount of \$410.00 for the above listed fees;
- payment of the following fees associated with this communication or credit any overpayment;
- any additional filing fees required under 37 CFR 1.16 including fees for presentation of extra claims; and
- any additional patent application processing fees under 37 CFR 1.17 and under 37 CFR 1.20 (d).

Triplicate copies of this transmittal are enclosed.

Date: December 4, 2001


Donna T. Ward
Registration No. 48,271
Isis Pharmaceuticals, Inc.

Please address all correspondence to:

Jane Massey Licata or Kathleen A. Tyrrell
Licata & Tyrrell, P.C.
66 East Main Street
Marlton NJ 08053
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Figure 1 consists of 12 sub-graphs labeled (a) through (l). Each graph plots a physiological parameter against time (0 to 10 minutes). The y-axis for all graphs ranges from 0 to 100. The x-axis for all graphs ranges from 0 to 10 minutes. The graphs show that HR, SV, CO, MAP, PVR, SVR, PPA, and PVP all increase during the intervention period, while PVP/PPA remains relatively stable.

- (a) HR (b/min): Baseline ~60, Intervention ~80.
- (b) SV (ml): Baseline ~50, Intervention ~70.
- (c) CO (l/min): Baseline ~3.0, Intervention ~4.5.
- (d) MAP (mmHg): Baseline ~70, Intervention ~85.
- (e) PVR (mmHg): Baseline ~10, Intervention ~25.
- (f) SVR (mmHg): Baseline ~15, Intervention ~30.
- (g) PPA (mmHg): Baseline ~10, Intervention ~25.
- (h) PVP (mmHg): Baseline ~10, Intervention ~25.
- (i) PVP/PPA: Baseline ~1.0, Intervention ~1.0.
- (j) PVP/PPA: Baseline ~1.0, Intervention ~1.0.
- (k) PVP/PPA: Baseline ~1.0, Intervention ~1.0.
- (l) PVP/PPA: Baseline ~1.0, Intervention ~1.0.

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Inventor(s): Alexander H. Borchers and Kenneth W. Dobie

Serial No.: not yet assigned Filing Date: herewith

Title: Antisense Modulation of Hematopoietic cell protein tyrosine kinase Expression

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Assistant Commissioner for Patents
Washington, D.C., 20231

STATEMENT TO SUPPORT FILING AND SUBMISSION IN ACCORDANCE WITH 37 C.F.R. §§
1.821 THROUGH 1.825

I hereby state, in accordance with the requirements of 37 C.F.R. §1.821(f), that the contents of the paper and computer readable copies of the Sequence Listing, submitted in accordance with 37 C.F.R. §1.821(c) and (e), respectively, are the same.

Date: December 4, 2001

Respectfully submitted,


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